1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bravecto 112.5 mg Chewable Tablets Veterinary
Bravecto 250 mg Chewable Tablets Veterinary
Bravecto 500 mg Chewable Tablets Veterinary
Bravecto 1000 mg Chewable Tablets Veterinary
Bravecto 1400 mg Chewable Tablets Veterinary

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:
Each chewable tablet contains:

Bravecto chewable tablets	**Fluralaner (mg)**
for very small dogs (2–4.5 kg)	112.5
for small dogs (>4.5–10 kg)	250
for medium-sized dogs (>10–20 kg)	500
for large dogs (>20–40 kg)	1,000
for very large dogs (>40–56 kg)	1,400

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Chewable tablet.
Light to dark brown tablet with a smooth or slightly rough surface and circular shape. Some marbling, speckles or both may be visible.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs

4.2 Indications for use, specifying the target species

For the treatment of tick and flea infestations in dogs.

This veterinary medicinal product is a systemic insecticide and acaricide that provides:
- immediate and persistent flea (*Ctenocephalides felis*) killing activity for 12 weeks,
- immediate and persistent tick killing activity for 12 weeks for *Ixodes ricinus, Dermacentor reticulatus* and *D. variabilis,*
- immediate and persistent tick killing activity for 8 weeks for *Rhipicephalus sanguineus*.

Fleas and ticks must attach to the host and commence feeding in order to be exposed to the active substance. The onset of effect is within 8 hours of attachment for fleas (*C. felis*) and 12 hours of attachment for ticks (*I. ricinus*).

The product can be used as part of a treatment strategy for the control of flea allergy dermatitis (FAD).

For the treatment of demodicosis caused by *Demodex canis*.
For the treatment of sarcoptic mange (*Sarcoptes scabiei* var. *canis*) infestation.

4.3 Contraindications

Do not use in case of hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings for each target species

Parasites need to start feeding on the host to become exposed to fluralaner; therefore the risk of the transmission of parasite borne diseases cannot be excluded.

4.5 Special precautions for use

Special precautions for use in animals

Use with caution in dogs with pre-existing epilepsy.

In the absence of available data, the veterinary medicinal product should not be used on puppies less than 8 weeks old and /or dogs weighing less than 2 kg.

The product should not be administered at intervals shorter than 8 weeks as the safety for shorter intervals has not been tested.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

Keep the product in the original packaging until use, in order to prevent children from getting direct access to the product.

Hypersensitivity reactions in humans have been reported.

Do not eat, drink or smoke while handling the product.

Wash hands thoroughly with soap and water immediately after use of the product.

4.6 Adverse reactions (frequency and seriousness)

Mild and transient gastrointestinal effects such as diarrhoea, vomiting, inappetence, and drooling were commonly observed in clinical trials (1.6% of treated dogs).

Lethargy, muscle tremor, ataxia and convulsions have been reported very rarely in spontaneous reports.

Most reported adverse reactions were self-limiting and of short duration.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s)
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form
https://sideeffects.health.gov.il/

4.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product in breeding, pregnant and lactating dogs has been demonstrated. Can be used in breeding, pregnant and lactating dogs.

4.8 Interaction with other medicinal products and other forms of interaction

Fluralaner is highly bound to plasma proteins and might compete with other highly bound active substances such as non-steroidal anti-inflammatory drugs (NSAIDs) and the cumarin derivative warfarin. Incubation of fluralaner in the presence of carprofen or warfarin in dog plasma at maximum expected plasma concentrations did not reduce the protein binding of fluralaner, carprofen or warfarin.

During clinical field testing, no interactions between Bravecto chewable tablets for dogs and routinely used veterinary medicinal products were observed.

4.9 Amounts to be administered and administration route

For oral use.

Bravecto should be administered in accordance with the following table (corresponding to a dose of 25–56 mg fluralaner/kg bodyweight within one weight band):

Bodyweight of dog (kg)	**Strength and number of tablets to be administered**				
	Bravecto 112.5 mg	Bravecto 250 mg	Bravecto 500 mg	Bravecto 1000 mg	Bravecto 1400 mg
2–4.5	1				
>4.5–10		1			
>10 -–20			1		
>20–40				1	
>40 –56					1

The chewable tablets should not be broken or divided.
For dogs above 56 kg bodyweight, use a combination of two tablets that most closely matches the bodyweight.

Method of administration:
Administer Bravecto chewable tablets at or around the time of feeding.
Bravecto is a chewable tablet and is well accepted by most dogs. If the tablet is not taken up voluntarily by the dog it can also be given with food or directly into the mouth. The dog should be observed during administration to confirm that the tablet is swallowed.

Treatment schedule:
For optimal control of flea infestation, the veterinary medicinal product should be administered at intervals of 12 weeks. For optimal control of tick infestation, the timing of retreatment depends on the tick species. See section 4.2.

For the treatment of *Demodex canis* mite infestations, a single dose of the product should be administered. As demodicosis is a multi-factorial disease, it is advisable to also treat any underlying disease appropriately.
For the treatment of sarcoptic mange infestations (*Sarcoptes scabiei* var. *canis*), a single dose of the product should be administered. The need for and frequency of re-treatment should be in accordance with the advice of the prescribing veterinarian.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

No adverse reactions were observed following oral administration to puppies aged 8–9 weeks and weighing 2.0–3.6 kg treated with overdoses of up to 5 times the maximum recommended dose (56 mg, 168 mg and 280 mg fluralaner/kg bodyweight) on three occasions at shorter intervals than recommended (8-week intervals).

There were no findings on reproductive performance and no findings of concern on offspring viability when fluralaner was administered orally to Beagle dogs at overdoses of up to 3 times the maximum recommended dose (up to 168 mg/kg bodyweight of fluralaner).

The veterinary medicinal product was well tolerated in Collies with a deficient multidrug-resistance-protein 1 (MDR1 -/-) following single oral administration at 3 times the recommended dose (168 mg/kg bodyweight). No treatment-related clinical signs were observed.

4.11 Withdrawal period

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Ectoparasiticides for systemic use.
ATCvet code: QP53BE02.

5.1 Pharmacodynamic properties

Fluralaner is an acaricide and insecticide. It is efficacious against ticks (*Ixodes* spp., *Dermacentor* spp. and *Rhipicephalus sanguineus*), fleas (*Ctenocephalides* spp.), *Demodex canis* mites and sarcoptic mange (*Sarcoptes scabiei* var. *canis*) on the dog.

Fluralaner has a high potency against ticks and fleas by exposure via feeding, i.e. it is systemically active on target parasites.

Fluralaner is a potent inhibitor of parts of the arthropod nervous system by acting antagonistically on ligand-gated chloride channels (GABA-receptor and glutamate-receptor).

In molecular on-target studies on insect GABA receptors of flea and fly, fluralaner is not affected by dieldrin resistance.

In *in vitro* bio-assays, fluralaner is not affected by proven field resistances against amidines (tick), organophosphates (tick, mite), cyclodienes (tick, flea, fly), macrocyclic lactones (sea lice), phenylpyrazoles (tick, flea), benzophenyl ureas (tick), pyrethroids (tick, mite) and carbamates (mite).

The product contributes towards the control of the environmental flea populations in areas to which treated dogs have access.

Newly emerged fleas on a dog are killed before viable eggs are produced. An *in vitro* study also demonstrated that very low concentrations of fluralaner stop the production of viable eggs by fleas. The flea life cycle is broken due to the rapid onset of action and long lasting efficacy against adult fleas on the animal and the absence of viable egg production.

5.2 Pharmacokinetic particulars

Following oral administration, fluralaner is readily absorbed reaching maximum plasma concentrations within 1 day. Food enhances the absorption. Fluralaner is systemically distributed and reaches the highest concentrations in fat, followed by liver, kidney and muscle. The prolonged persistence and slow elimination from plasma ($t_{1/2}$ = 12 days) and the lack of extensive metabolism provide effective concentrations of fluralaner for the duration of the inter-dosing interval. Individual variation in C_{max} and $t_{1/2}$ was observed. The major route of elimination is the excretion of unchanged fluralaner in faeces (~90% of the dose). Renal clearance is the minor route of elimination.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Super premium in powder for dog flavor
Sucrose
Maize starch
Sodium lauryl sulfate
Disodium pamoate monohydrate
Magnesium stearate
Aspartame
Glycerol
Soya-bean oil (0.1% BHT stabilized)
Macrogol 3350

6.2 Major incompatibilities

None known.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4. Special precautions for storage

Store below 25°C.

6.5 Nature and composition of immediate packaging

Cardboard box with 1 aluminium foil blister sealed with PET aluminium foil lid stock containing 1, 2 or 4 chewable tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of as toxic waste, do not throw to sewer.

7. LICENSES NUMBERS

Bravecto 112.5 mg Chewable Tablets Veterinary - 156-03-34344-00
Bravecto 250 mg Chewable Tablets Veterinary - 156-04-34346-00
Bravecto 500 mg Chewable Tablets Veterinary - 156-05-34347-00
Bravecto 1000 mg Chewable Tablets Veterinary - 156-06-34348-00
Bravecto 1400 mg Chewable Tablets Veterinary - 156-07-34349-00

8. MANUFACTURER

Intervet GesmbH
Siemensstrasse 107
1210 Vienna
Austria

9. MARKETING AUTHORISATION HOLDER:

Intervet Israel Ltd.
Neve Ne'Eman Industrial Park
Hod HaSharon 45240

Revised in July 2022 according to MOHs guidelines.